Clinical, laboratory, microbiological and echocardiographic characteristics of infective endocarditis in a tertiary care hospital

ANA G. MÚNERA-ECHEVERRI, CAROLINA SALDARRIAGA-ACEVEDO • MEDELLÍN (COLOMBIA)

DOI: https://doi.org/10.36104/amc.2021.1930

Abstract

Objectives: infective endocarditis (IE) is a potentially fatal disease. This study analyzed the clinical, laboratory, microbiological and echocardiographic characteristics of IE in a population of patients at a tertiary care hospital in Medellín, Colombia, over a three-year period.

Methods: a retrospective observational study. The patients were classified according to the modified Duke criteria. Clinical and echocardiographic data, laboratory results and cultures were gathered from the clinical charts. Factors associated with the prognosis were determined.

Results: a total of 48 cases were included, 29 (60.4%) of which involved males. The mean age was 53.8±19.2 years. Fever and fatigue were the most common clinical signs. No heart murmur was reported on admission in 52.1% of the patients. Most of the patients (62.5%) had no underlying predisposing heart condition. The IE occurred in a native valve in 36 patients (75%), with the mitral valve being the most frequently affected site. Transthoracic and/or transesophageal echocardiography showed vegetations in 45 cases (93.7%); these were mostly mobile, with an average size of 17.6±11.3 mm. *Staphylococcus aureus* was the main causal organism (33%). The prevalence of IE with negative blood cultures was 37.5%. The most frequent complication was embolism in 21 patients (43.7%), followed by heart failure (41.7%). On multivariate analysis, septic shock, kidney failure, *Staphylococcus* infection and the use of immunosuppressants were predictors of higher inpatient mortality.

Conclusions: most cases occur in elderly patients with no underlying predisposing heart condition, in a native valve, with a predilection for the mitral valve. *Staphylococcus aureus* is the most frequent causal organism. Several factors predict greater inpatient mortality, including the presence of septic shock, kidney failure, *Staphylococcus* infection and the use of immunosuppressants. **(Acta Med Colomb 2021; 46. DOI: https://doi.org/10.36104/amc.2021.1930)**

Keywords: *endocarditis, echocardiography, epidemiology, heart valves, Staphylococcus*.

Dra. Ana G. Múnera-Echeverri: Internista, Cardióloga, Ecocardiografista. Servicio de Cardiología No Invasiva Hospital General de Medellín. Investigador Grupo HGM y Docente Universidad CES; Dra. Carolina Saldarriaga-Acevedo: Cardióloga, Fellow de Ecocardiografía Universidad CES. Medellín (Colombia).
Correspondencia: Dra. Ana G. Múnera-Echeverri. Medellín (Colombia).
E-Mail: anagm@une.net.co
Received: 26/VI/2020 Accepted:19/V/2021

Introduction

Infective endocarditis (IE) is a difficult and complex disease. Despite advances in its diagnosis and medical and surgical treatment, IE continues to be associated with high mortality and serious complications (1).

The epidemiological profile of IE has changed substantially over the last few years (2, 3). Historically, it affected young patients with underlying predisposing valve disease, predominantly rheumatic, and *Streptococcus viridans* was the most frequent pathogen (4). Over the last few years, the age of patients with IE has increased and degenerative valve disease is the most common predisposing lesion in developed countries where rheumatic fever has ceased to be a public health problem. The number of patients with IE and no prior known history of valve disease has also increased considerably (5). The microbiology has also changed, with many recent studies reporting that *Staphylococcus aureus is currently the main causative microorganism of IE (6, 7)*.

Numerous studies have evaluated the clinical, microbiological and echocardiographic characteristics of IE in the Western world. However, little is known regarding the epidemiology of IE in our setting, its echocardiographic characteristics, the main microbiological agents involved, the most common clinical manifestations and the complications in our patients. The local behavior of this entity must be observed in order to determine if there is a difference in the clinical profile which could serve as a basis for developing future management strategies.

This study analyzes the clinical, laboratory, microbiological and echocardiographic characteristics of IE in a group

of patients at a tertiary care hospital in Medellín, Colombia over a period of three years.

Materials and methods

This was designed as a retrospective observational study. All patients over the age of 18 with a diagnosis of IE in their medical chart and seen by the echocardiography service at Hospital General de Medellin between March 2011 and June 2014 were included.

Data were collected from the medical charts regarding demographic characteristics, age, sex, underlying heart disease, presenting signs and symptoms, comorbidities, laboratory and microbiology results, echocardiographic findings, the need for surgery and complications.

All patients met the following requirements: 1. Over the age of 18 years, 2. Definitive or probable diagnosis of IE according to the modified Duke criteria, 3. Transthoracic and/or transesophageal two-dimensional echocardiography, and 4. Serial blood cultures.

Definition of terms

1. According to the modified Duke criteria:

Major criteria

- Positive blood cultures: a typical microorganism consistent with IE from two separate blood cultures, or a microorganism consistent with IE from persistently positive blood cultures, or a single positive blood culture for *Coxiella burnetti* or IgG antibody titers > 1:800.
- Echocardiographic evidence of endocardial involvement with the presence of vegetations, an abscess, a fistula, a pseudoaneurysm or a new dehiscence of a prosthetic valve; abnormal activity around a prosthetic valve on positron emission tomography (PET/CT) or single-photon emission computerized tomography (SPECT/CT) or paravalvular lesions on cardiac computerized tomography.

Minor criteria

- Predisposing conditions such as underlying heart disease or the use of intravenous drugs, fever, vascular phenomena, immunological phenomena and positive blood cultures not classified as a major criterion.

Definitive IE: two major criteria, or one major and three minor criteria, or five minor criteria.

Possible IE: one major criterion and one minor criterion, or three minor criteria.

Safety and ethical considerations

According to Article 11 of Resolution 008430 of 1993 issued by the Ministry of Health of the Republic of Colombia, this project is classified as a no-risk study, since retrospective documentary techniques and methods are used; no intentional intervention of the individuals' physiological, psychological, biological or social variables was performed as the source of data was the medical chart, fulfilling, in turn, Resolution 8430 of 1993, issued by the Ministry of Health, which establishes the scientific, technical and administrative norms for healthcare research.

The data on each of the patients' variables were entered into a Microsoft Excel spreadsheet. The statistical analysis of the results was performed with SPSS version 21 software. Quantitative variables are presented with measures of central tendency (average) and dispersion (standard deviation). Categorical variables are presented as proportions. The bivariate analysis included the Chi square test for categorical variables and Student's t-test or Mann-Whitney U for quantitative variables. The confidence level for the hypothesis tests was 95%. The relationship between the size of vegetations and complications was analyzed using the Chi square test. Factors associated with inpatient mortality were analyzed through binary logistic regression, using a forward stepwise method. A p value less than 0.05 was considered statistically significant for all statistical analyses.

Results

Of the 48 cases included, 46 patients (95.8%) were classified as definitive endocarditis and two patients (4.2%) as probable endocarditis according to the modified Duke criteria.

The patients' main characteristics are shown in Table 1; 29 patients (60.4%) were men, and 19 patients (39.6%) were women, with a 1.5:1 male to female ratio. The average age (±SD) was 53.8±19.2 years.

Native valve endocarditis occurred in 36 patients (75%), prosthetic valve endocarditis in three patients (6.3%) and endocarditis associated with an intracardiac device in nine patients (18.8%). With regard to how they acquired the infection, 20 patients (42%) had healthcare-related endocarditis and 28 patients (58%) had community-acquired endocarditis. Most patients had no underlying predisposing heart condition (62.5%).

Fever and fatigue were the patients' most common clinical manifestations (70.8 and 77.1%, respectively). A heart murmur was reported as a clinical finding in 47.9% of the patients (Table 2).

Thirty cases (62.5%) had positive blood cultures and 18 (37.5%) had negative blood cultures. Of the latter, one patient had a microbiological diagnosis with a valve tissue culture.

Table 3 summarizes the causative microorganisms of the infection during the study. *Staphylococcus* was the cause in 39.6% of cases and *Streptococcus* in 14.5%. *S. aureus* was isolated in 16 patients (33%) and was the most frequent microorganism, followed by *Streptococcus sanguis in three patients* (6.3%).

The initial diagnosis was made by transesophageal echocardiography in 26 patients (54.2%) and by transthoracic echocardiography in 22 (45.8%). The mean time between the clinical suspicion and the first echocardiogram was 24

Table 1. *Baseline characteristics of patients with infective endocarditis (IE).*

Variables	n=48
Baseline characteristics at diagnosis	
Male sex, *n (%)*	29 (60.4)
Age, X (DS)	53.8 (19.2)
Comorbidities, n (%)	
Arterial hypertension	24 (50)
Diabetes mellitus	8 (16.7)
Chronic kidney disease	9 (18.8)
Malignancy	4 (8.3)
Prior IE	1 (2.1)
Valve disease	8 (16.6)
Aortic regurgitation	2 (4.1)
Mitral regurgitation	4 (8.3)
Mitral valve prolapse	1 (2.1)
Double mitral lesion	1 (2.1)
Congenital heart disease	7 (14.6)
Bicuspid aorta	1 (2.1)
VSD	3 (6.2)
PDA	1 (2.1)
Subaortic membrane	1 (2.1)
AV canal	1 (2.1)
Prosthetic valve	3 (6.3)
Biological	3 (6.3)
Mechanical	0 (0)
Intracardiac device	6 (12.5)
Inflammatory diseases	7 (14.5)
Intravenous drug use	0 (0)
HIV	1 (2.1)
Use of steroids or other immunosuppressants	6 (12.5)

IE: infective endocarditis, VSD: ventricular septal defect, PDA: patent ductus arteriosus, AV: atrioventricular, HIV: human immunodeficiency virus.

Table 2. *Clinical manifestations of patients with infective endocarditis.*

Clinical manifestations	n (%)
Fever	34 (70.8)
Fatigue	37 (77.1)
Dyspnea	25 (52.1)
Chills	31 (64.6)
Seizures/neurological focalization	5 (10.4)
Gastrointestinal symptoms	15 (31)
Chest pain	6 (12.5)
Headache	8 (16.7)
Weight loss	12 (25)
Muscle/joint symptoms	21 (43.8)
Skin lesions	15 (31.3)
Murmur	23 (47.9)

hours (15-48 hours). Forty-one patients required only one echocardiogram for diagnosis, seven patients required two echocardiograms for diagnosis. The main echocardiographic findings are summarized in Table 4. Vegetations were found in 45 of the 48 patients (93.7%), most were mobile (40/45, 88.8%), and the mitral valve was the most frequent location (17/45, 37.7%), followed by the aortic valve (16/45, 35.5%). The average size of the vegetations was 17.6±11.3 mm. The most frequent complication was embolism in 21 patients (43.7%), followed by heart failure in 41.7%. The most common sites of embolism were the lung and central nervous system (CNS) (nine and eight cases, respectively) (Table 5).

A statistically significant association was found between *Staphylococcus* infection and pulmonary embolism (p=0.01), but not CNS embolism (p= 0.390).

There was no statistically significant association between the location of the vegetation and embolism. Out of 17 patients with mitral valve endocarditis, eight had an embolism (47%); out of 16 patients with aortic valve endocarditis, eight had an embolism (50%); out of 10 patients with endocarditis related to device cables or catheters, four embolized (40%); and out of six patients with tricuspid valve endocarditis, two embolized (33%).

Patients with mobile vegetations tended to have more complications, although the relationship was not statistically significant, except for heart failure (p=0.04) (Table 6). Out of eight patients with CNS emboli, seven (87.5%) had mobile vegetations, and only one patient had non-mobile vegetations. Out of nine patients with pulmonary emboli, eight (88.8%) had mobile vegetations and only one had non-mobile vegetations. One hundred percent of patients with valve perforation as a complication had mobile vegetations.

Most patients had ≥10 mm diameter vegetations (35 patients); of these, 100% had an embolic complication. Of the patients with <10 mm vegetations (10 patients), only three had an embolus, although this relationship did not reach statistical significance.

A statistically significant relationship was found between the size of the vegetations (≥10 mm) and paravalvular leaks (p=0.03) and prosthetic dehiscence (p=0.03).

Among the patients' baseline characteristics, advanced age (over 55 years) was statistically significantly associated

Table 3. *Microorganism isolated.*

Microbiology	
Staphylococcus	19 (39.6)
Methicillin-sensitive Staphylococcus aureus	13
Methicillin-resistant Staphylococcus aureus	3
CNS	3
Enterococcus	2 (4.1)
1: *E. faecalis*	2
2: *E. faecium*	0
Streptococcus	7 (14.5)
Streptococcus viridans	1
Streptococcus bovis	0
Other species of *Streptococci*	1
Streptococcus gallolyticus	1
Streptococcus sanguis	3
Streptococcus mitis	1
Gram negative organisms	2 (4.1)
Brucella	0
Pseudomonas aeruginosa	0
HACEK group	0
Serratia marcescens	1
Klebsiella pneumoniae	1
Candida	1 (2.1)
Candida albicans	0
Candida tropicalis	1
Candida parapsilosis	0

CNS: Coagulase-negative *Staphylococcus*, HACEK: *Haemophilus parainfluenzae, Actinobacillus, Cardiobacterium, Eikenella corrodens and Kingella kingae.*

Table 4. *Echocardiographic findings.*

Vegetations, *n (%)*	45 (93.7)
Maximum size in mm (±SD) Number of vegetations	17.6 (11.3)
1	24 (53.3)
2	11 (24.4)
3	10 (22.2)
Mobile Location	40 (88.8)
Aortic	16 (35,5)
Mitral	17 (37.7)
Tricuspid	6 (13.3)
Intracavitary	3 (6.6)
Device cables or catheters	10 (22.2)
Common AV valve	1 (2.2)
Pulmonary	1 (2.2)
Aortic regurgitation	21 (43.7)
Mitral regurgitation	29 (60.4)
Tricuspid regurgitation	22 (45.8)
Pulmonary regurgitation	3 (6.3)
LVEF%	60 (46 – 65)
PASP mmHg	45 (38 – 58)
LVEF: left ventricular ejection fraction, PASP: pulmonary artery systolic pressure, AV: atrioventricular	

with the risk of peripheral embolism (p=0.04); other variables analyzed, such as diabetes mellitus, arterial hypertension or kidney failure were not significantly associated with emboli.

Heart failure was a complication in 20 patients, 19 with native valve endocarditis. Of these, 11 patients had aortic valve vegetations and eight patients had mitral valve vegetations.

There were two cases of aortic root abscess in patients with native valve endocarditis. In one, *E. faecalis was isolated, and in the other, S. lugdunensis*.

Perivalvular extension occurred in four patients with native valve endocarditis, with aortic valve (2), tricuspid valve (1) and intracavitary (1) vegetations. *Staphylococcus* was isolated in three patients and *E. faecalis* in one.

Eleven cases of valve perforation were found, seven involving the mitral valve and four the aortic valve. The most commonly involved germ in these cases was *S. aureus* (36.4%).

Using multivariate analysis, a significant association was found between mortality as an outcome and septic shock, kidney failure, *Staphylococcus* infection and the use of immunosuppressants. No association was found with the other variables analyzed (Table 7).

Discussion

Although the incidence of IE in the general population was not analyzed, the results indicate that despite advances in health care, IE continues to pose a diagnostic and therapeutic challenge for physicians, especially now that the pattern of presentation differs substantially from that of a few years ago. Those at greatest risk of infection are no longer young patients with known rheumatic valve disease; now they are older people with no apparent valve disease (5, 8). In this study, most patients did not have a predisposing underlying heart condition (62.5%), just as reported by Castillo et al. in an epidemiological study in Spain, where in the last seven years, 64% of the IE cases were patients with no predisposing heart disease (5).

The average age of onset was 53.8±19.2 years. The increase in the age of patients with IE coincides with other

Table 5. *Complications of patients with infective endocarditis.*

Complications	
Aortic root abscess, *n (%)*	2 (4.2)
Pseudoaneurysm	0
Valve aneurysm	0
Perforation	11 (22.9)
Fistula	1 (2.1)
Paravalvular leak	2 (4.2)
Prosthetic dehiscence	2 (4.2)
Valve destruction	0
Rupture of chordae tendinae	3 (6.3)
Pericardial effusion	15 (31.3)
Heart failure	20 (41.7)
Perivalvular extension	4 (8.3)
Embolism	21 (43.7)
Lung	9
CNS	8
Extremities	6
Spleen	2
Skin	2
Spondylodiscitis	1
Kidney	1
Septic shock	13 (27.1)
AV block	1 (2.1)
Kidney failure requiring renal replacement therapy	14 (29.2)
CNS: central nervous system, AV: atrioventricular.	

Table 6. *Vegetation mobility and complications.*

Vegetations and complications			
	Mobiles n (%)	**Non-mobile n (%)**	**P value**
CNS embolism	7 (87.5)	1 (12.5)	0.64
Perforation	11 (100)	0 (0)	0.22
Paravalvular leak	1 (100)	0 (0)	0.88
Pericardial effusion	14 (93.3)	1 (6.7)	0.45
Heart failure	20 (100)	0 (0)	0.04
CNS: central nervous system			

Table 7. *Factors associated with inpatient mortality: multivariate analysis.*

Multivariate analysis			
Variable	**P value**	**Exp (B)**	**95% CI**
Septic shock	0.005	14.91	(2.30- 96.49)
Kidney failure with RRT	0.033	6.57	(1.16- 37.22)
Staphylococcus	0.048	5.11	(1.01- 25.79)
Inmunosuppressants	0.047	9.37	(1.03- 85.24)
RRT: renal replacement therapy.			

studies carried out within the last decade (9, 10). This could be explained by greater survival of the population and by the increased number of IE cases related to hospitalization and health care. As in the vast majority of studies, we found a predominance in males, with a male: female ratio of 1.5:1 (5, 6, 11).

Our study confirmed many clinical characteristics of endocarditis which occur in other parts of the world. For example, most of the IE cases were in native valves (75%) and the mitral valve was most commonly affected, followed by the aortic valve (10, 11).

Infective endocarditis with negative blood cultures may occur in up to 31% of IE cases, and often poses a considerable diagnostic and treatment challenge. It occurs most frequently due to prior antibiotic use, highlighting the need to suspend the antibiotics and repeat the blood cultures in this situation (12). In this study, we found a 37.5% prevalence of IE with negative blood cultures.

The published studies disagree on which causative microorganism is the most frequent; this variation may be related to the study population (10, 11, 14, 15). The studies which include intravenous drug users report a higher prevalence of *S. aureus* as the causative agent; other studies predominantly include patients with prosthetic valve IE. According to reports from recent studies, the *Staphylococcus* species have surpassed *Streptococcus* species as the most frequent causative microorganism of native valve IE (12, 13). In this study, which predominantly included native valve IE cases, with no intravenous drug use cases, the *Staphylococcus* species were the most frequent (39.6%), especially *Staphylococcus aureus* (33%), followed by *Streptococcus* species (14.5%), indicating that the globally reported shift from *S. viridans as the main germ* in the past to *S. aureus* currently, is also true in our study population and is probably related to the same reasons, such as a growing number of invasive procedures (vascular catheters, intracardiac devices, etc.).

The most common presenting symptoms were fatigue and fever; however, the prevalence of fever in our study was lower than that reported by other authors (12). A total

of 29.2% of the patients did not report a fever, which suggests that the lack of fever should not exclude a diagnosis of IE in a patient with suggestive clinical characteristics.

The lack of a murmur in patients with IE has been described previously; however, the proportion of cases without a murmur (52.1%) was much greater in our study than what was reported in a retrospective study by Fefer P. et al. (16).

Echocardiography was the cornerstone of IE diagnosis in our study. Vegetations were found in most cases (93.7%). The size of the vegetations (17.6 ± 11.3 mm) was much greater in our study than what was reported in a Spanish registry by Roca B. et al. (17), in which the average length was 9 mm. Mitral regurgitation was the predominant heart condition in our study (60.4%), similar to what was reported by Winston and Bolger (18).

The prevalence of embolism was high in our study (43.7%), coinciding with what was published previously by Vilacost et al. (19). The most frequent sites of embolism were the lung (42.8%) and the central nervous system (38%). The prevalence of spleen embolism was much lower than that reported in the literature, and this may reflect an underdiagnosis due to fewer abdominal imaging studies being routinely performed on these patients (12).

Several observational studies have evaluated the relationship between the location of vegetations on the echocardiogram and the risk of complications (19-21), finding that vegetations on the mitral valve are a risk factor for embolism. In this study, we did not find a statistically significant relationship between the location of the vegetations and embolism, with a similar proportion of emboli in patients with mitral and aortic valve vegetations. Mobile vegetations were associated with a greater incidence of complications like embolism, although this association did not reach statistical significance in our study, perhaps due to the size of the sample.

As previously mentioned, the size of the vegetations in this study was much larger than what was reported in other studies; vegetations which were ≥10 mm had more frequent

The multivariate analysis showed an increased risk of death from endocarditis in the presence of septic shock, kidney failure, *Staphylococcus* infection and the use of immunosuppressants. Other studies on this aspect have reached similar conclusions as ours regarding the factors associated with greater mortality (22-25). However, there are also studies which have found a significant association of other factors with mortality, such as heart failure and advanced age (26). The discrepancies may be explained by the different study designs and the lack of uniformity in the analyzed variables.

Our study has several limitations, especially the sample size, its retrospective design and the low number of serological and molecular tests performed, which limits the detection of fastidious organisms such as *Brucella, Bartonella, Coxiella* and other rare causes of IE which cannot be ruled out with traditional microbiological studies.

This study provides an epidemiological profile of IE in Medellín, Colombia. Although this study included 48 patients over a period of three years in a tertiary care hospital, this frequency is comparable to or greater than that reported in other studies, such as that of Senior (27), in which 92 patients were included over a longer period (11 years) and from three reference centers, and that of Olaya Sánchez et al. (28) with 34 patients in four years. The sizes of these studies are explained by the low prevalence of infective endocarditis.

Conclusions

This study shows the epidemiological, clinical and echocardiographic characteristics of a population with IE in a tertiary care hospital in Medellín, Colombia. In our population, IE is currently a disease which predominantly affects older people without predisposing underlying heart disease. Most of the cases are native valve endocarditis, with greater involvement of the mitral valve. *S. aureus* was the most frequent causative microorganism. Echocardiography is the cornerstone of diagnosis. This study helps recognize the prognostic factors which identify patients at higher risk of inpatient mortality in our population.

Source of Support

Universidad CES.

Acknowledgements

Special thanks to Dr. Elsa María Vásquez Trespalacios for her help with the statistical analysis in this study. To Universidad CES and to Hospital General de Medellín.

References

1. **Mylonakis E, Calderwood SB.** Infective endocarditis in adults. *N Engl J Med* 2001;345: 1318-30.
2. **Netzer RO, Zollinger E, Seiler C, Cerny A.** Infective endocarditis: Clinical spectrum, presentation and outcome. An analysis of 212 cases 1980-1995. *Heart* 2000;84:25-30.
3. **Tleyjeh IM, Steckelberg JM.** Changing Epidemiology of Infective Endocarditis. Curr Infect Dis Reports 2006;8:265-70.
4. **Griffin MR, Wilson WR, Edwards WD, O'Fallon WM, Kurland LT**. Infective endocarditis: Olmsted County. Minnesota. *JAMA* 1985;254: 1199–202.
5. **Castillo JC, Anguita M, Ruiz M, Pena L, Santisteban M. y col.** Changing Epidemiology of Native Valve Infective Endocarditis. *Rev Esp Cardiol*. 2011;64(7):594–598
6. **Hill EE, Herijgers P, Claus P, Vanderschueren S, Herregods MC, Peetermans WE.** Infective endocarditis: changing epidemiology and predictors of 6-month mortality: a prospective cohort study. *Eur Heart J*. 2007;28:196–203.
7. **Cabell CH, Jollis JG, Peterson GE, Corey GR, Anderson DJ, Sexton DJ, et al.** Changing patient characteristics and the effect on mortality in endocarditis. *Arch Intern Med*. 2002;162:90–4.
8. **Strom BL, Abrutyn E, Berlin JA, Kinman JL, Feldman RS, Stolley PD, et al**. Dental and Cardiac Risk Factors for Infective Endocarditis. A Population-Based, Case-Control Study. *Ann Intern Med* 1998;129: 761-9.
9. **Tuğcu A, Yıldırımtürk Ö, Baytaroğlu C, Kurtoğlu H, Köse Ö, Şener M, et al.** Clinical spectrum, presentation, an risk factors for mortality in infective endocarditis: A review of 68 cases at a tertiary care center in Turkey. *Turk Kardiyol Dern Ars* 2009;37: 9-18.
10. **Murdoch DR, Corey GR, Hoen B, Miro JM, Fowler VG, Bayer AS, et al.** Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century. *Arch Intern Med* 2009;169: 463-73.
11. **Ferreiros E, Nacinovich F, Casabe JH, Modenesi JC, Swieszkowski S, Cortl C, et al.** Epidemiologic, clinical and microbiologic profile of infective endocarditis in Argentina: a national survey. The Endocarditis Infecciosa en la Republica Argentina-2 Study. *Am Heart J*. 2006;151:545–52.
12. **Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti**

F, et al. 2015 ESC Guidelines for the management of infective endocarditis. The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). *European Heart Journal*. First published online: 29 August 2015

13. **Barrau K, Boulamery A, Imbert G, Casalta JP, Habib G, Messana T, et al**. Causative organisms of infective endocarditis according to host status. *Clin Microbiol Infect* 2004;10: 302-8.
14. **Tleyjeh IM, Steckelberg JM, Murad HS, Anavekar NS, Ghomrawi HM, Mirzoyev Z, et al.** Temporal trends in infective endocarditis. A population-based study in Olmsted County. *JAMA*. 2005;293: 3022–8.
15. **Hoen B, Alla F, Selton-Suty C, Beginot I, Bouvet A, Briancon S, et al.** Changing profile of infective endocarditis: results of a 1-year survey in France. *JAMA*. 2002;288: 75–81.
16. **Fefer P, Raveh D, Rudensky B, Schlesinger Y, Yinnon AM.** Changing epidemiology of infective endocarditis: a retrospective survey of 108 cases, 1990-1999. *Eur J Clin Microbiol Infect Dis* 2002;21:432-7.
17. **Roca B, Marco JM.** Presentation and outcome of infective endocarditis in Spain: a retrospective study. International Journal of Infectious Diseases (2007) 11, 198-203
18. **Winston LG, Bolger AF.** Modern epidemiology, prophylaxis, and diagnosis and therapy for infective endocarditis. *Curr Cardiol Rep* 2006;8:102-8.
19. **Vilacosta I, Graupner C, San Roman JA, Sarria C, Ronderos R, Fernandez C, Mancini L, Sanz O, Sanmartin JV, Stoermann W.** Risk of embolization after institution of antibiotic therapy for infective endocarditis. *J Am Coll Cardiol* 2002;39:1489–1495.
20. **Rohmann S, Erbel R, Gorge G, Makowski T, Mohr-Kahaly S, Nixdorff U, Drexler M, Meyer J**. Clinical relevance of vegetation localization by transoesophageal echocardiography in infective endocarditis. *Eur Heart J* 1992;13:446–452.
21. **Sanfilippo AJ, Picard MH, Newell JB, Rosas E, Davidoff R, Thomas JD, Weyman AE.** Echocardiographic assessment of patients with infectious endocarditis: prediction of risk for complications. *J Am Coll Cardiol* 1991;18:1191–1199
22. **Leone S, Ravasio V, Durante-Mangoni E, Crapis M, Carosi G, Scotton PG, Barzaghi, N, Falcone M, Chinello P, Pasticci MB, Grossi P, Utili R, Viale P, Rizzi M, Suter F.** Epidemiology, characteristics, and outcome of infective endocarditis in Italy: the Italian Study on Endocarditis. Infection 2012;40:527–535.
23. **Olmos C, Vilacosta I, Fernandez C, Lopez J, Sarria C, Ferrera C, Revilla A, Silva J, Vivas D, Gonzalez I, San Roman JA**. Contemporary epidemiology and prognosis of septic shock in infective endocarditis. *Eur Heart J* 2013;34:1999–2006.
24. **Chu VH, Cabell CH, Benjamin Jr DK, Kuniholm EF, Fowler Jr VG, Engemann J, et al.** Early predictors of in-hospital death in infective endocarditis. *Circulation* 2004;109:1745-9.
25. **Casabe JH, Deschle H, Cortes C, Stutzbach P, Hershson A, Nagel C, et al.** Predictors of hospital mortality in 186 cases of active infective endocarditis treated in a tertiary medical center (1992-2001). *Rev Esp Cardiol* 2003;56:578-85.
26. **Netzer R, Altwegg SC, Zollinger S, Täuber M, Carrel T, Seiler C.** Infective endocarditis: determinants of long term outcome. *Heart* 2002;88:61–66
27. **Senior JM.** Endocarditis infecciosa. Descripción clínico-epidemiológica. *Acta Med Colomb* 1995; **20**(4):169-75
28. **Olaya Sánchez A, Vargas Vergara D, Montes Zabala L, Avila Cortéz Y, Cárcamo Molina LM.** Descripción clínica, microbiológica y ecocardiográfica de la endocarditis infecciosa en un hospital de Bogotá durante los años 2013-2017. *Acta Med Colomb* 2019; 44(4)